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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/183,055      | 10/29/1998  | CARL H. JUNE         | 36119-125US8        | 2710             |

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03/06/2003

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 03/06/2003

28

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/183055

Applicant(s)

JUNE

Examiner

GAMBEL

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 4/1/02 ; 7/10/01
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1, 46, 47, 54-58, 69-72 is/are pending in the application.
- 4a) Of the above claim(s) 1, 46, 47, 54-58, 69-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1, 46, 47, 54-58, 69-72 is/are allowed.
- 6) ☒ Claim(s) 1, 46, 47, 54-58, 69-72 is/are rejected.
- 7) ☐ Claim(s) 1, 46, 47, 54-58, 69-72 is/are objected to.
- 8) ☐ Claim(s) 1, 46, 47, 54-58, 69-72 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 1/1/02 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on 1/1/02 is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. 09/183055.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 09/183055
- 4) ☐ Interview Summary (PTO-413) Paper No(s) 09/183055
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

1. Applicant's submission, filed 7/10/02 (Paper No. 27), has placed this application in compliance with the Sequence Rules.

2. Applicant's amendment, filed 4/1/02 (Paper No. 25), has been entered.

Claims 1, 46-47, 54-58 and 69-72 are pending.

Claims 2-45, 48-53 and 59-68 have been canceled previously.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Office Action will be in response to applicant's arguments, filed 4/1/02 (Paper No. 25).

The rejections of record can be found in the previous Office Action (Paper No. 18).

4. Applicant is reminded to amend the first line of the specification to update the relationship and status of the priority documents.

Applicant's amended priority, filed 4/1/02 (Paper No. 25), does not provide the relationship and status of all of the priority documents for the instant application.

Applicant's amendment to delete the priority to USSN 07/275,433, filed 11/23/88, is acknowledged.

5. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 1, 46, 47 and 56-58 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed for the reasons of record set forth in Paper No. 18.

Applicant's arguments, filed 4/1/02 (Paper No. 25), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 18.

Applicant aver that the invention, as claimed, was conceived at the time of filing of the application.

Applicant aver that the skilled artisan would have known the critical common structural attributes of a ligand for CD9 other than CD9-specific antibodies, namely the ability of the ligand to bind to and stimulate a CD9 molecule on the surface of a CD8<sup>+</sup> T cell. Further applicant asserts that the skilled artisan would have understood that an anti-CD9 antibody is merely a non-example (non-limiting example) of such a CD9 ligand.

The following of record is reiterated for applicant's convenience.

There is insufficient written description encompassing a "ligand which binds the accessory molecule CD9" because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of both the "ligand", are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

It does not appear that the specification as filed provides sufficient written description for a ligand other than CD9-specific antibodies that would provide the specificity and activity required by the claimed CD9-specific ligands in the claimed methods.

It does not appear that the specification as filed provides sufficient written description for the critical common structural attributes of a ligand other than CD9-specific antibodies.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species or a single species (anti-CD9 antibodies) to support an entire genus. The instant invention encompasses targeting CD9 with any ligand, yet the instant specification does not provide sufficient written description as to the structural features of said ligands and the correlation between the chemical structure and the function of the genus of ligands other than anti-CD9 antibodies. The reliance on the disclosed limited example of anti-CD9 antibodies does not support the written description of any ligand. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological activities. Therefore, structurally unrelated ligands other than anti-CD9 antibodies encompassed by the claimed invention would be expected to have greater differences in their structures, expression and activities.

A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences for identifying a ligand, encompassed by the claimed invention. There is insufficient guidance based on the reliance of anti CD9 antibodies to direct a person of skill in the art to select or to predict particular sequences as essential for identifying any ligand, encompassed by the claimed invention. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

The instant claims do not provide functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of ligands, and because the genus is highly variable, anti-CD9 antibodies are insufficient to describe the genus of CD9-specific ligands encompassed by the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of ligands and CD9 ligands, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant's arguments are not found persuasive.

6. Claims 1, 46, 47 and 56-58 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "anti-CD9 antibodies" as CD9-specific ligands, does not reasonably provide enablement for any "CD9-specific ligand" to be employed in the claimed methods for the reasons of record set forth in the previous Office Action (Paper No. 18).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments, filed 4/1/02 (Paper No. 25), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 18.

Applicant argues that the ordinary artisan would have known that the anti-CD9 antibodies described in the specification was a non-limiting example. Applicant asserts that the skilled artisan would have known that any structural characteristics of a CD9-binding ligand, aside from those features necessary to allow binding to CD9, are irrelevant to applicant's invention. Applicant asserts that regardless of its structural characteristics, falls within the claimed invention so long as it actually binds to and stimulates CD9.

The following of record is reiterated for applicant's convenience.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies CD9-specific ligands other than those encompassed by "anti-CD9 antibodies" as disclosed in the specification as filed and set forth in claim 69 for example. CD9 ligand may have some notion of the activity of the receptor and ligand, claiming biochemical molecules by a particular name given to the protein (e.g receptor or ligand) by various workers in the field fails to distinctly claim what that protein is and what the compositions are made up of. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any ligand for CD9.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species to support an entire genus. The instant invention encompasses any CD9-specific ligand, yet the instant specification does not provide sufficient guidance and direction as to the structural features of said CD9 ligands and the correlation between the chemical structure and the desired CD9 ligand. The reliance on the disclosed limited example of "anti-CD9 antibodies" does not support the enablement for any CD9 ligand.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species or a single species of anti-CD9 antibodies to support an entire genus. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological properties. Therefore, structurally unrelated ligands encompassed by the claimed invention other than "anti-CD9 antibodies" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. ligand or receptor) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence or a limited number of species and in turn utilizing predicted structural determinations to ascertain binding or functional aspects ligands and receptors and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Because of the lack of sufficient guidance and predictability in determining which structures would lead to CD9 ligands with the desired structural and functional properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of ligand and receptors encompassed by the claimed invention.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance upon the CD9-specific antibodies does not appear to provide sufficient enabling support for any ligand or CD9 and so the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Without sufficient guidance, making and using CD9 ligands would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant's arguments are not found persuasive.

7. Claims 1, 46, 47, and 54-58 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 46, 47 and 54-58 are indefinite in they appear to be incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. For example, the claims lacks the activating and stimulating steps.

Applicant should specifically point out the support for any amendments made to the disclosure.  
See MPEP 714.02 and 2163.06

Applicant asserts that the mere addition of an anti-CD3 antibody to a population of T cells will necessarily stimulate the T cells and the CD9 accessory molecule on the T cells is stimulated upon binding by that molecule by a CD9 binding ligand.

Applicant's arguments have been fully considered but are not found convincing for the reasons of record and reiterated herein above.

8. Claims 1, 46, 47, and 54-58 and 69-72 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,858,358 (June et al.) for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims, as they read on stimulating the proliferation of T cells, including CD8<sup>+</sup> T cells, appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of CD3-specific and CD9-specific antibodies

Applicant request that this ground of rejection be held in abeyance until the claims are deemed allowable. Applicant will file a terminal disclaimer, if a double patenting rejection exists at that time.

9. No claim is allowed.

The instant claims appear to be free of the art, other than the obvious double patenting rejection set forth herein.




**10. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

  
Phillip Gambel, PhD.  
Primary Examiner  
Technology Center 1600  
March 5, 2003